Protective Effect of N-Acetylcysteine Against Toxicity on the Rat Blood After Chronic Exposure to Carbosulfan
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Abstract
The present study investigated the protective effects of N-acetylcysteine (NAC), widely known as an antidote to acetaminophen overdose, on carbosulfan (CB)-induced hematotoxicity and oxidative stress in male rats. CB was administered at a dose of 25 mg/kg or simultaneously administered with NAC (2 g/l) for 30 days. Results of hematological examination showed that red blood cells, hematocrit, hemoglobin, and reticulocytes levels were significantly lower in CB-exposed rats compared with those in the control. Administration of CB caused a significant increase in the superoxide dismutase and catalase activities. However, the glutathione (GSH) and thiols group (TSH) levels were significantly increased as well as GSH S-transferase activity and levels of glutathione peroxidase on erythrocytes of males rats compared with those in the control. Also, CB-treated rats showed significant elevation in lipid peroxidation (LPO) and acetylcholinesterase (AChE) on erythrocytes in comparison with the control. Co-administration with NAC exhibited chemoprotective effects against CB-mediated hematotoxicity, augmented erythrocyte antioxidant status, and prevented the induction of anemia.

Keywords: N-acetylcysteine; Carbosulfan; Rat erythrocyte; Oxidative stress.

1. INTRODUCTION
Pesticides are occasionally used indiscriminately in large amounts causing environmental pollution and, therefore, are a cause of concern. Residual amounts of carbamates pesticides have been detected in the soil, water bodies, vegetables, grains, and other foods products (Abdollahi et al., 2004). Carbamates are known to cause inhibition of acetylcholinesterase (AChE) activity in the target tissues (Abdollahi et al., 1996) which accumulates acetylcholine and prevents the smooth transmission of nerve functions leading to convulsions and death. However, low intakes of carbamate through food and water may not show clear symptoms of OP intoxication such as convulsions but it may show mild inhibition of AChE activity in erythrocytes and tissues. Recent studies indicate that carbosulfan (CB) intoxication produce oxidative stress by the generation of free radicals and induce lipid peroxidation (LPO) in the rat spleen (El-Bini Dhouib et al., 2014) and in the fish liver (Capkin et al., 2014). As some of the carbamates may be present in blood of exposed humans and animals, it may produce oxidative stress in erythrocytes. The antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) as well as total-SH content in erythrocytes, however, may neutralize the oxidative stress. N-acetylcysteine (NAC) is a cysteine prodrug and can be considered a GSH precursor (Rushworth and Megson, 2014) and oral administration of NAC replenishes the cellular levels of GSH (Atkuri et al., 2007). High-dose oral of NAC is an effective antioxidant and as it is present at the site of free radical generation, it may neutralize the toxic effects of reactive oxygen species (ROS) (Aruoma et al., 1989).

It has not been studied whether NAC modify the alterations induced by CB in antioxidant enzyme system and LPO concentrations in the rat erythrocyte. Hence, we aimed to evaluate whether there would be protective effect of NAC on hematological parameters, oxidative stress, and antioxidants values in CB-induced hematotoxicity in rats.

2. MATERIALS AND METHODS

2.1. Animals
Rats (Wistar, 100-150 g of weight and 45 days of age) procured from Tunisian Society of Pharmaceutical Industries, divided into two groups, and housed two per cage in sterile plastic cage. The vivarium was maintained under normal day/night schedule (12 h light/12 h dark cycles) at room temperature 25°C ± 1°C. Balanced food and water were given to the animals ad libitum. All the procedures were in accordance with Guidelines for Ethical Conduct in the Care and Use of Animals.

2.2. Chemical
CB was provided by Tunisian Ministry of Agriculture; before use CB was dissolved in corn oil for a final concentration 25 mg/ml.
2.3. Treatment Schedule
The rats were randomly divided into three groups of 12 animals each. The first group (control group: CTR) received orally 1 ml corn oil via stomach tube daily during 30 days. The second group (CB) received an amount of 1 ml corn oil containing 25 mg of CB/kg body weight/day. The last group (NAC) received 25 mg of CB/kg body weight/day and 2 g/l of N-acetylcysteine (C$_5$H$_9$–NO$_3$S) in drinking water. The choice of CB dose was based on previous experimental assays in our laboratory, which corresponds to an acceptable dose that did not cause any sign of toxicity until the end of the experiments. This dose corresponds to 20% of LD50 for rat (Umetsu and Fukuto, 1982).

The dose of NAC was selected on the basis of previously published reports suggesting that NAC was not toxic to humans or animals at this dose (Ortolani et al., 2000). Furthermore, NAC does not show any signs of toxicity at doses even higher than the one administered in the present study (El Midaoui et al., 2008).

2.4. Blood Collection
At day 30 and 2 h after the last dose, blood was collected from the retro-orbital plexus of each rat using heparinized capillary tubes for determination of the Acetylcholinesterase (AChE) activity and EDTA (Ethylene Tetra Acetic Acid) tubes for hematological parameters determination. The blood was centrifuged and the erythrocytes were washed twice with 0.1 M phosphate buffered saline (PBS, 1:9), pH 7.4. Erythrocyte lysate was prepared according to the method of McCord and Fridovich (1969) for the assay of oxidative stress parameters (Mates et al., 1999b).

2.5. Acetylcholinesterase Activity in Erythrocytes
AChE activity was assayed by the method of Ellman et al. (1961). Hemoglobin (Hb) was estimated using Drabkin’s reagent by the method of Dacie and Lewis (1968).

2.6. Determination of Blood Cellularity
Blood samples were analyzed immediately for blood cellularity using an automatic hematological assay analyzer (BC-2800 VET Mindray Auto Hematology Analyzer, Mindray, China). Routine hematological parameters were assessed: RBC (Red Blood Cell), Hb (Hemoglobin), Ht (Hematocrite), MCV (Mean Corpuscular Volume), MCH (Mean Corpuscular Hemoglobin), MCHC (Mean Corpuscular Hemoglobin Concentration), and Reticulocytes.

2.7. Lipid peroxidation
LPO is detected by the determination of malondialdehyde (MDA) production determined by the method of Begue and Aust (1978). Erythrocytes were centrifuged at 10,000 × g for 10 min at 4°C to sediment cell debris and mitochondrial samples, were suspended in PBS (0.1 M; pH 7.4), mixed with BHT–TCA (butylhydroxytoluene, trichloroacetic acid) solution (1% (w/v) BHT dissolved in 20% TCA) and centrifuged at 3000 × g for 35 min. Then, the supernatant was mixed with 0.5 NaCl and 120 mM TBA (thiobarbituric acid) in 26 mM Tris and heated in water bath at 80°C for 10 min. After cooling, we determined the absorbance of the resulting chromophore at 532 nm. MDA levels were determined by using an extinction coefficient for MDA–TBA complex of 1.56 × 10$^5$ M$^{-1}$ cm$^{-1}$.

2.8. Determination of Thiol Groups Concentration
Erythrocytes are added to 0.25 M base Tris and 20 mM EDTA pH 8.2 (Hu and Dillard, 1994). Then, the mixture was vortexed and its absorbance was determined at 412 nm. The first value was noted A1. After that, 10 mM DTNB (5,5-dithiobis, 2-nitrobenzoate) were added and incubated for an incubation period of 15 min and a new value A2 was determined. The white tube of DTNB contains only DTNB and buffer; its absorbance value is noted as B. We calculated the concentration of thiol groups (TSH) per tube by using this equation expression: (A2–A1–B) × 1.57 mM.

2.9. Antioxidant Enzymes Activities
The activity of SOD in erythrocytes of control and treated rats was assayed by the spectrophotometric method. CAT activity was measured at 20°C by a slightly modified method of Aebi (1984). Hydrogen peroxide ($\text{H}_2\text{O}_2$) decomposition by CAT enzyme was monitored kinetically at 240 nm. One unit of activity is equal to the micromole of $\text{H}_2\text{O}_2$ degraded per minute per milligram of Hb.

2.10. Glutathione and Related Enzymes
Total glutathione (GSH) content in tissue was measured by the method of Tietze (1969) using dithionitrobenzene and expressed as mmol/ml. Glutathione peroxidase (GPx) activity was measured by the Wendel method, using tertbutylhydroperoxide as a substrate (Wendel, 1981). Nicotinamide adenine dinucleotide phosphate (NADPH) disappearance was monitored by a spectrophotometer at 340 nm. Glutathione S-transferase (GST) activity was assayed by the procedure of Habig et al. (1974) using 1-chloro-2,4-dinitrobenzene (CDNB) as a substrate. The assay was conducted by monitoring the appearance of the conjugated complex of CDNB and GSH at 340 nm.
2.11. Statistical Analysis
Data were statistically analyzed using the Student “t” test to determine significant differences between different groups. 
*p* values less than 0.05 were considered significant. The values are expressed as means ± SD.

3. RESULTS

3.1. Influence of NAC on the CB-Induced Hematotoxicity
The mean values of hematological parameters in rats exposed to CB alone and CB plus NAC are presented in Table 1. Rats administered with CB had significant alteration in RBCs, Hb, hematocrit, and reticulocytes values when compared with those in the control group. Co-administration with NAC significantly increased the values of RBC, Hb, and reticulocytes values to near CB group.

3.2. Erythrocyte AChE Activity
AChE activity in erythrocyte is shown in Figure 1. There was a significant decrease in AChE activity by 43.78% after 30 days treatment (*p* < 0.01) in CB-treated group. On the other hand, NAC treatment resulted in partial recovery of AChE activity (127.7%) in erythrocyte as compared to the CB treated animals.

3.3. Erythrocyte Oxidative Stress

3.3.1. LPO
Effect of *in vivo* the co-administration of CB and NAC on the LPO levels in the erythrocytes are presented in Figure 2. CB treatment resulted in a significant decrease in MDA level (30.9%) as compared to the control animals. On the other hand, NAC treatment resulted in a partial recovery of MDA level (127.5%) as compared to the CB-treated animals.

Table 1: Effect of NAC on CB-induced hematotoxicity in rats following 30 days exposure.

<table>
<thead>
<tr>
<th></th>
<th>CTR</th>
<th>CB</th>
<th>NAC</th>
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</thead>
<tbody>
<tr>
<td>RBC (10¹²/l)</td>
<td>6.7 ± 1.01</td>
<td>8.278 ± 0.829</td>
<td>8.036 ± 0.551</td>
</tr>
<tr>
<td>Hb (g/l)</td>
<td>131.8 ± 12.39</td>
<td>160.333 ± 3.617*</td>
<td>144.5 ± 5.779*b</td>
</tr>
<tr>
<td>Ht (%)</td>
<td>39.78 ± 4.38</td>
<td>48.1 ± 1.677c</td>
<td>46.35 ± 2.371</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>61.3 ± 4.753</td>
<td>60.06 ± 4.853c</td>
<td>60.1 ± 2.971</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>18.4 ± 1.37</td>
<td>17.6 ± 0.41</td>
<td>18.35 ± 1.675</td>
</tr>
<tr>
<td>MCHC (g/l)</td>
<td>323.25 ± 10</td>
<td>313.7 ± 2.495</td>
<td>317.666 ± 3.747</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
<td>2.98 ± 0.23</td>
<td>1.36 ± 0.15&amp;a</td>
<td>2.5 ± 0.22*b</td>
</tr>
</tbody>
</table>

CTR: control group; CB: treated group with CB; NAC: treated group with CB and supplemented with NAC. Values are expressed as mean ± SD (*n* = 12).

*a* Significantly different from the control group (*p* < 0.05).

*b* Significantly different from the CB group (*p* < 0.05).

Figure 1: Effect of NAC on AChE activity in erythrocytes of CB-exposed rats following 30 days exposure.

CTR: control group; CB: treated group with CB; NAC: treated group with CB and supplemented with N-acetylcysteine. Values are expressed as mean ± SD (*n* = 12). *a* Significantly different from the control group (*p* < 0.05). *b* Significantly different from the CB group (*p* < 0.05).
**Figure 2: Effect of NAC on MDA activity in erythrocytes of CB-exposed rats following 30 days exposure.**
CTR: control group; CB: treated group with CB; NAC: treated group with CB and supplemented with N-acetylcysteine. Values are expressed as mean ± SD (n = 12). *Significantly different from the control group (p < 0.05). †Significantly different from the CB group (p < 0.05).

**Figure 3: Effect of NAC on TSH content in erythrocytes of CB-exposed rats following 30 days exposure.**
CTR: control group; CB: treated group with CB; NAC: treated group with CB and supplemented with N-acetylcysteine. Values are expressed as mean ± SD (n = 12). *Significantly different from the control group (p < 0.05). †Significantly different from the CB group (p < 0.05).

**Figure 4: Effect of NAC on GSH level in erythrocytes of CB-exposed rats following 30 days exposure.**
CTR: control group; CB: treated group with CB; NAC: treated group with CB and supplemented with N-acetylcysteine. Values are expressed as mean ± SD (n = 12). *Significantly different from the control group (p < 0.05). †Significantly different from the CB group (p < 0.05).
Table 2: Effect of NAC on levels of antioxidant enzymes (SOD and CAT) and on the activity of glutathione peroxidase (GPx) and glutathione S-transferase (GST) in erythrocytes of CB-exposed rats following 30 days exposure.

<table>
<thead>
<tr>
<th></th>
<th>CTR</th>
<th>CB</th>
<th>NAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD (U/mg of Hb)</td>
<td>0.49 ± 0.022</td>
<td>0.65 ± 0.022*</td>
<td>0.48 ± 0.022*</td>
</tr>
<tr>
<td>CAT (U/mg of Hb)</td>
<td>0.576 ± 0.115</td>
<td>2.476 ± 0.573*</td>
<td>0.882 ± 0.222*</td>
</tr>
<tr>
<td>GPx (nmol oxidized GSH min/mg of Hb)</td>
<td>66.987 ± 5.263</td>
<td>41.658 ± 3.541*</td>
<td>59.485 ± 5.74*</td>
</tr>
<tr>
<td>GST (nmol of conjugated CDNB min/mg of Hb)</td>
<td>125.542 ± 7.365</td>
<td>95.234 ± 5.214*</td>
<td>110.1 ± 3.47*</td>
</tr>
</tbody>
</table>

CTR: control group; CB: treated group with CB; NAC: treated group with CB and supplemented with NAC. Values are expressed as mean ± SD (n = 12).
*Significantly different from the control group (p < 0.05).
#Significantly different from the CB group (p < 0.05).

3.3.2. GSH and total thiol content
GSH and total thiol contents of various groups are depicted in Figures 3 and 4. In case of CB-treated animals, there was a significant decrease in the GSH content (88.23%) as compared to the control group. NAC treatment protected against CB-induced reduction in GSH levels (162.35%) in the rat erythrocyte as evident by an increase in GSH content. Total thiol content was significantly decreased in the erythrocyte of CB treated animals (66.87%) as compared to the control animals. NAC treatment to the CB-exposed animals significantly increased the TSH content (143.75%) as compared to the CB-treated animals.

3.3.3. Antioxidant enzymes
The effects of CB and NAC co-administration on the activity of the antioxidant enzymes are reported in Table 2. CB induced a significant (p < 0.05) increase in SOD and CAT activities versus a decrease in GPx and GST activities. Nevertheless, NAC, supplemented in drinking water, caused a dramatic decrease in SOD and CAT activities and an increase in GPx and GST activities of rats supplemented with NAC until CB treated values.

4. DISCUSSION
The uncontrolled exposure to toxic pesticides, such as CB, is capable of inflicting biological damage leading to the pathology of many conditions including blood disorders. In the present investigation, administration of CB caused significant alterations in some hematological parameters. The significant alteration in the number of RBC, Hb, hematocrit, and reticulocytes in this experimental model indicates that exposure to CB could lead to bleeding anemia. Our findings on CB treatment-related hematological toxicity are in agreement with the report on rats exposed to CB (43 mg/kg) (Kandil et al., 2006). The co-administration with NAC significantly improved hematological parameters by restoring to normalcy the RBC number, Hb level, and reticulocytes percentage. Our results corroborate with those of Cuzzocrea et al. (2001), they showed that NAC, in vivo, NAC significantly prevent RBC alteration and prevent the loss of Hb content.

It is well-known that AChE is irreversibly inhibited by carbamates insecticides by carbamylation (O’Malley, 1997). Once a given molecule of cholinesterase has been inhibited reversible, the only way of replacing the activity is though synthesis of new enzyme. The synthesis does not occur in circulating RBCs and only way RBC-AChE is renewed in the blood is through synthesis of enzyme in erythropoietic cells of the bone-marrow and its subsequent entry into the circulating blood (Abdollahi et al., 1999; Gordon and Rowsy, 1998). Therefore, measurement of erythrocyte AChE activity can be a marker of chronic exposure to carbamates pesticides anti-AChEs (O’Malley, 1997). Our results revealed that CB alone caused a statistically significant decrease (43.78%) in the activity of AChE in erythrocytes of male rats compared to the control results (Figure 1). The treatment with NAC increases AChE activity. Also, when AChE is reversibly inhibited in erythrocytes, the recovery toward normal values depends on new cell entering the bloodstream, and has been calculated for most organophosphorus pesticides to correspond to 1%/day (Gordon and Rowsy, 1998).

LPO has been suggested as one of the molecular mechanisms involved in organophosphorus and carbamate pesticide-induced toxicity (Kehrer, 1993). Malondialdehyde (MDA) level in CB treatment was significantly (p ≤ 0.05) higher than that in control group and the change accounted to 30.9% in male rats (Figure 2). These indirectly suggest an increased production of oxygen free radicals in rats. Highly reactive oxygen metabolites, especially hydroxyl radicals, act on unsaturated fatty acids of phospholipid components of membranes to produce malondialdehyde, a LPO product. Carbamates pesticides have been reported to induce oxidative stress, as shown by enhanced MDA production (Amer et al., 2002; Eraslan et al., 2009; Mansour et al., 2009; Rai et al., 2009). The use of NAC in conjunction with CB affected such elevation in the level of MDA; bringing it within the normal limits (p ≤ 0.05–0.01). The normalization
of LPO following NAC treatment is very likely due to its antiperoxidative properties, as has been shown previously by Zafarullah et al. (2003) and Thorin-Trescases et al. (2010). NAC plays an important role in regulation of cellular GSH that is vital to cellular antioxidant defense (Lucht et al., 1987). It has also been reported to interact with cell membranes to stabilize them against various damaging effects, including those due to oxidative injuries (Zhang et al., 1990). Also, GSH-dependent defense against xenobiotics is a multifaceted phenomenon that has been well characterized in mammals. CB exposure decreased GSH content in the erythrocyte. Our findings are in accordance with those of Soderpalm-Berndes and Onfelt (1988), who have reported lowering of GSH levels by carbaryl. The mechanism involved in GSH depletion after carbamate exposure involves carbamylation of TSH (Ningaraj et al., 1998). The decrease in GSH levels might diminish the overall antioxidant potential of the erythrocyte resulting in increased LPO following CB exposure. GSH depletion may also effect the activation and translocation of transcription factors like NF-kB and c-Jun/activating transcription factor (Rokutan et al., 1998). NAC administration was seen to augment GSH levels and confer its protective effects in CB hematotoxicity. The decreased TSH content on CB exposure rats might be contributed by reduction in GSH levels and/or could be due to decrease in protein thiol groups.

Elevation in the level of MDA, aftereffect of CB administration, result in dysfunction and the question of whether oxidative stress is a major cause of erythrocyte injury remains equivocal. However, the antioxidant enzymes SOD, GST, and CAT limit the effects of oxidant molecules on tissues and are active in the defense against oxidative cell injury by means of their being free radical scavengers (Kyle et al., 1987). These enzymes work together to eliminate active oxygen species and small deviations in physiological concentrations may have a dramatic effect on the resistance of cellular lipids, proteins, and DNA to oxidative damage. The enzymatic antioxidants in erythrocytes can counteract oxidative stress. For instance, SOD catalyzes the conversion of superoxide radical to hydrogen peroxide, while CAT converts hydrogen peroxide to water. These antioxidant enzymes can, therefore, alleviate the toxic effects of ROS (Mates and Sanchez-Jimenez, 1999a; Mates et al., 1999b). Moreover, the existence of a mutually supportive relationship between metalloenzyme SOD, which accelerates the dismutation of endogenous cytotoxic superoxide radicals to H$_2$O$_2$, and CAT, which converts the deleterious peroxide radicals into water and oxygen, provides the first line of defense to the cells (Adedara and Farombi, 2010). The increased activities of erythrocyte SOD and CAT observed in CB-treated animals may lead to decreased steady-state levels of the deleterious superoxide radicals and H$_2$O$_2$.

In fact, hydroxyl radical could be formed by the interaction of superoxide radical with H$_2$O$_2$ through the Haber–Weiss reaction (Adedara et al., 2013). The overwhelming generation of free radicals in the blood milieu may contribute to the inactivation of these enzymes and may increase the oxidative stress in erythrocyte of animals treated with CB. These findings were in line with the previous reports, showing a decrease in free radical scavenger enzyme activities in rats exposed to carbofuran, principal metabolite of CB (Mansour et al., 2009; Rai et al., 2009). However, we found a decrease in the GPx and GST activities in CB-treated groups (Table 2). These data could be explained by an increase in ROS formation and oxidative stress induction. This finding is not rare. Indeed, similar results were observed in rats treated with carbamate pesticide (Fukuto, 1990; Abdollahi et al., 2004; Mansour et al., 2009).

However, amelioration was evident by marked increases in the SOD and CAT activities in erythrocyte of animals co-treated with NAC in comparison with those of CB-treated animals. As with other antioxidant enzymes, NAC was found to protect GPx from carbofuran. Farbiszewski et al. have also found protective effect of NAC on GPX activity in methanol intoxicated rats (Farbiszewski et al., 2000). The present results may indicate that there was a quick scavenging of superoxide and hydroxyl radicals by NAC, possibly due to its high bioavailability, to keep their normal levels, thereby allowing the erythrocyte antioxidant system to efficiently decrease CB-mediated erythrocyte ROS generation. The ability of NAC to inhibit hydroxyl and superoxide anion radicals in vitro has been reported by Zachwieja et al. (2005).

In summary, severe oxidative stress can lead to hemolysis. In principle, the erythrocyte is very sensitive to peroxidative reactions. Under normal conditions, the erythrocyte is very well protected against peroxidative reactions by the presence of CAT and GSH. This balance, however, can be disturbed by different chemicals. Oxidative damage can result indirect injury to the cell membrane due to LPO and bring about changes in membrane proteins (i.e., enzymes) and consequently, the permeability of such membranes of any erythrocyte (Brkić et al., 2008). CB caused erythropenia and a reduction in the Ht and Hb levels. These results suggest existing of absolute anemia as a result of hemolytic or depression anemia (Jain, 1993). Surprisingly, the supplementation of NAC effectively attenuated the alterations induced by CB in the hematological variables and thereby protecting the heme from CB induced oxidative stress. CB might reduce the oxidative stress by scavenging the free radical and ROS by its effective antioxidative and free radical scavenging activities reported by El-bini Dhouib et al. (2014).

In mechanistic term, the presence of acetyl and sulfhydryl groups makes NAC a potent inhibitor of LPO. In addition, NAC is a thiol, a mucolytic agent, and a precursor of L-cysteine and reduced GSH. NAC is a source of sulfhydryl groups in cells and scavenger of free radicals as it interacts with ROS such as OH and H$_2$O$_2$ (Aruoma et al., 1989). GSH is currently one of the most studied antioxidants as it is endogenously synthesized basically in all cells. Among many, established roles for GSH are the following: (i) antioxidant defense, (ii) detoxification of electrophilic xenobiotics, (iii) modulation of redox (oxidation–reduction reaction)-regulated signal transduction, and (iv) storage and transport of cysteine. GSH has an important role in maintaining the redox state of the cell (Kerkisch and Willoughby, 2005).
It thereby exerts a profound protective effect on cells. Of the three amino acids in the GSH structure (glutamate, glycine, and cysteine), cysteine has the lowest intracellular concentration (Aruoma et al., 1989). Cysteine availability can limit the rate of GSH synthesis during times of oxidative stress. NAC is an acetylated cysteine residue able to increase cell protection to oxidative stress. NAC is an effective scavenger of free radicals as well as a major contributor to maintenance of the cellular GSH status. NAC can minimize the oxidative effect of ROS through correcting or preventing GSH depletion (Kerksick and Willoughby, 2005).

Taken together, the data presented in this study clearly demonstrate, for the first time, that both NAC elicited significant protection against CB-mediated hematotoxicity. Moreover, NAC is efficient in protecting the erythrocyte from toxicity and oxidative damage induced by CB as evidenced by the restoration of antioxidant status and biomarkers of erythrocyte damage to normalcy. Also, NAC may be potential therapeutic tools for hematotoxicity resulting from CB exposure.

5. CONCLUSION

In view of the data of the present study, it can be concluded that CB-induced oxidative stress and LPO in erythrocytes of male rats and conjunction supplementation of NAC has ameliorated these effects. The precise mechanism of the observed protective effect of NAC cannot be ascertained from the results of this study and thus remains to be explored in future.

Author Contributions

All authors contributed equally to this work.

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